requested.

Attached hereto is an appendix entitled "Version with Markings to Show Changes Made" which depicts the changes made to the instant application by the current amendment.

Objections

Applicants acknowledge the Examiner's remarks concerning the Declaration. Accompanying this Amendment and Response is a new Declaration executed by inventor Andrew Chan, which correctly identifies U.S. Patent Application Serial No. 08/819,013 as patented and U.S. Patent Application Serial No. 08/788,322 as abandoned. We are presently awaiting a newly executed declaration from the second inventor, Chong Fu.

Applicants acknowledge the Examiner's objection to the incorporation by reference of subject matter deemed essential. The subject matter in question concerns the nature of high stringency conditions for hybridization, which is deemed essential because "high stringency conditions" is recited in the pending claims. Applicants point out that the pending claims have been cancelled, and that the new amended claims do not recite for BLNK proteins encoded by nucleic acids that will hybridize under high stringency conditions to other nucleic acids.

Applicants request withdrawal of the objections.

Rejections Under 35 U.S.C. §101

Claims 23-34 stand rejected under 35 U.S.C. §101 as lacking either a specific and substantial asserted utility or a well-established utility. The Examiner expresses that BLNK protein activity is not defined by the instant specification and that the utility asserted for BLNK protein by the instant specification is a general utility. Applicants traverse.

Applicants draw the Examiner's attention to the revised U.S. PTO Utility Examination Guidelines published in the Federal Register, vol. 66, No. 4. At page 1098 of the identified volume of the Federal Register, at section B, 2, (2), the guidelines state:

> An applicant need only provide one credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement.

Further, at page 1096 in response to comment 19, the Commissioner cites *Fujikawa v. Wattanasin*, 95 F. 3d 1559,1562, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996), which states:

> "[A] 'rigorous correlation' need not be shown in order to establish a practical utility; 'reasonable correlation' is sufficient."

Further, at page 1098, section B, 4, the guidelines state:

> Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be proved that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. Similarly, Office personnel must accept an opinion from a qualified expert that is based upon relevant facts whose accuracy is not being questioned: it is improper to disregard the opinion solely because of a disagreement over the significance or meaning of the facts offered.

The instant specification asserts a number of characteristics and functions for BLNK proteins that support that the claimed BLNK protein compositions have specific, substantial utility. For example, the instant specification asserts at page 6, lines 11-15 that BLNK protein is tyrosine phosphorylated by Syk following B cell receptor activation, and at page 20, lines 6-8 that BLNK protein binds to Grb2, PLCγ, Nck and Vav, and regulates calcium levels and modulates cytoskeletal organization, and at page 19, lines 28-29 that BLNK protein is critical for B cell receptor mediated response and B cell function. Applicants submit that these statements are credible and should be accepted.

The instant application also provides methods for using the claimed BLNK protein compositions, for example to screen for bioactive agents that are capable of modulating BLNK protein activity (page 23, lines 4-11).

Applicants submit that the asserted function of BLNK protein is specific, as the asserted binding activities and B cell regulation activities disclosed in the instant application are not properties shared by all proteins.

In addition, Applicants submit that the asserted utility of BLNK protein is

substantial, as the ability to modulate B cell function and to identify bioactive agents therefore is clearly desirable.

While Applicant submits the assertions of the specification should be accepted without any further discussion into their accuracy, Applicant further submits support of the accuracy of the assertions in the form of the enclosed Declaration under 1.132 (the declaration). In paragraph 5 of the declaration, the inventor Andrew Chan, Ph.D., representing one of ordinary skill in the art, declares that he would expect to be able to use the claimed BLNK protein compositions as provided for in the present application. Moreover, the declaration discusses data already of record which confirms the accuracy of the assertions made in the application. Specifically, the declaration shows that loss of BLNK gene function results in abnormal B cell function, supporting the assertion that BLNK protein is a modulator of B cell function and that the loss thereof results in a BLNK-mediated disorder, and that the claimed BLNK protein compositions have specific and substantial utility.

Claims 23-34 have been cancelled without prejudice, disclaimer or admission. New Claims 35-38 are directed to BLNK proteins comprising an amino acid sequence having at least about 95% identity to SEQ ID NO:1. Claims 36-38 are further directed to BLNK proteins comprising SEQ ID NO:1, BLNK proteins which will bind to specified BLNK protein binding partners, and BLNK proteins which lack specific tyrosine phosphorylation sites as set forth in SEQ ID NO:1, respectively.

Claims 39-41 are directed to BLNK proteins comprising an amino acid sequence having at least about 95% identity to the amino acid sequence encoded by SEQ ID NO:2. Claims 40 and 41 are further directed to BLNK proteins comprising an amino acid sequence encoded by SEQ ID NO:2, and BLNK proteins which will bind to specified BLNK protein binding partners, respectively.

Claim 42 is directed to a pharmaceutical composition comprising the BLNK protein according to any one of Claims 35-41.

Claim 43 is directed to an antibody that binds to the BLNK protein according to any one of Claims 35-41.

Claims 44 and 45 are directed to methods for using BLNK proteins which BLNK

proteins comprise an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in SEQ ID NO:1 and will bind to Grb2, PLCγ, Vav, or Nck. Claim 44 is directed to methods for screening for a bioactive agent that will bind to a BLNK protein, while Claim 45 is directed to methods for screening for a bioactive agent capable of modulating BLNK protein activity.

Applicants submit that the new claims satisfy the utility requirement of 35 U.S.C. §101 and request withdrawal of the rejection and allowance of the claims.

Rejections Under 35 U.S.C. §112, First Paragraph - How to Use

Claims 23-34 stand rejected under 35 U.S.C. §112, first paragraph as failing to teach the reasonably skilled artisan how to use the invention for a credible, specific and substantial utility. Applicants traverse.

As discussed above and supported by the accompanying declaration, Applicants submit that new Claims 35-45 satisfy the utility requirement of 35 U.S.C. §101. Accordingly, Applicants submit that a person of reasonable skill in the art would be able to use the invention in full scope of the claims for a credible, specific and substantial utility.

Applicants request withdrawal of the rejection and allowance of the new claims.

Rejections Under 35 U.S.C. §112, First Paragraph - Written Description

Claims 23-34 stand rejected under 35 U.S.C. §112, first paragraph as lacking written description support in the specification. Applicants traverse.

The Office Action expresses that Claims 23-34 are directed to a very large genus of recombinant polypeptide species, uses thereof, and antibodies that bind thereto.

Claims 23-34 have been cancelled without prejudice, disclaimer or admission.

Applicants have amended the claims to further define the scope of the claimed BLNK protein compositions. Claims 35-38 are directed to BLNK proteins comprising an amino acid sequence having at least about 95% identity to SEQ ID NO:1. Claims 36-38 are further directed to BLNK proteins comprising SEQ ID NO:1, BLNK proteins which will bind to specified BLNK protein binding partners, and BLNK proteins which lack

specific tyrosine phosphorylation sites as set forth in SEQ ID NO:1, respectively.

Claims 39-41 are directed to BLNK proteins comprising an amino acid sequence having at least about 95% identity to the amino acid sequence encoded by SEQ ID NO:2. Claims 40 and 41 are further directed to BLNK proteins comprising an amino acid sequence encoded by SEQ ID NO:2, and BLNK proteins which will bind to specified BLNK protein binding partners, respectively.

Claim 42 is directed to a pharmaceutical composition comprising the BLNK protein according to any one of Claims 35-41.

Claim 43 is directed to an antibody that binds to the BLNK protein according to any one of Claims 35-41.

Claims 44 and 45 are directed to methods for using BLNK proteins which BLNK proteins comprise an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in SEQ ID NO:1 and will bind to Grb2, PLCγ, Vav, or Nck. Claim 44 is directed to methods for screening for a bioactive agent that will bind to a BLNK protein, while Claim 45 is directed to methods for screening for a bioactive agent capable of modulating BLNK protein activity.

The Office Action expresses at page 5 that the instant specification does not provide sufficient teaching or guidance for one of reasonable skill in the art to determine sequences that are within the scope of 95% identity to SEQ ID NO:1 and SEQ ID NO:2. The Examiner asserts that because no specific algorithm is disclosed, the claims do not find written description support in the specification. Applicants disagree.

Applicants point out that specific algorithms are disclosed in the instant specification. At page 24, lines 6-7, the instant application states: "All references cited herein are incorporated by reference."

Further, at page 5, line 12, the specification cites the prior art of Altschul et. al., J. Mol. Biol. 215:403-410, 1990 (Altschul-A) (a copy of which is attached as Exhibit A). Altschul-A describes the basic local alignment search tool (BLAST) and at page 404, left column, paragraph 3 discloses parameters for measuring nucleic acid similarity.

Altschul-A also discloses the prior art of Altschul et. al., J. Mol. Biol. 219:555-565, 1991 (Altschul-B) (a copy of which is attached as Exhibit B). Altschul-B discloses

the PAM-120 amino acid substitution matrix and scoring parameters therefore. The PAM-120 matrix and parameters are found at page 560, Table 4.

Accordingly, Applicants submit that the present application does properly disclose sequence comparison algorithms.

Applicants submit that one of ordinary skill in the art would clearly construe the meaning of 95% sequence identity based on the teaching of the specification and the knowledge held in the art, and would conclude that Applicants were in possession of the claimed BLNK protein compositions at the time of filing of the priority application.

Applicants submit that Claims 35-45 satisfy the written description requirement of 35 U.S.C. §112, first paragraph and request withdrawal of the rejection and allowance of the claims.

Rejections Under 35 U.S.C. §112, Second Paragraph - Indefiniteness

Claims 1-22, 23, 25, 27-28, and 31-34 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite. In particular, Claims 23, 25, 27-28 and 31-34, under consideration in the case, are found indefinite for use of the following phrases:

i) "polypeptide comprising the protein" (Claim 23);

ii) "high stringency conditions" (Claim 25 and 28); and

iii) "polypeptide" (Claims 27, 31-33).

As a preliminary matter, Applicants point out that Claims 23-34 have been cancelled without prejudice, disclaimer or admission.

New Claims 35-44 do not recite for proteins encoded by nucleic acids that will hybridize under high stringency conditions.

Applicants request withdrawal of the rejection and allowance of the new claims.

CONCLUSION

Applicants submit that the application is now in form for allowance and early notification of such is requested. If there remain issues that the Examiner believes may be resolved by telephone, he/she is respectfully requested to contact the undersigned at (415)

781-1989.

Respectfully submitted,

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